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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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საქართველოს სამედიცინო სიახლენი

## GEORGIAN MEDICAL NEWS

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**GMN: Georgian Medical News** is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.
GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

**GMN: Медицинские новости Грузии -** ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

**GMN: Georgian Medical News –** საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.
ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

**WEBSITE**

www.geomednews.com

## К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

**При нарушении указанных правил статьи не рассматриваются**.

## REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ,რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

*Содержание:*

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# A NOVEL NON-INVASIVE MODULATION OF ORTHODONTIC RELAPSE: INSIGHTS FROM A RABBIT MODEL

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## Abstract.

**Aim:** Low-intensity pulsed ultrasound (LIPUS), such as Exogen device, stimulates osteogenesis and angiogenesis without harmful thermal effects, enhancing bone strength and shortening recovery time. This experimental study evaluated the application of Exogen low-intensity pulsed ultrasound (LIPUS) device in promoting alveolar bone healing and reducing post-orthodontic relapse in rabbits model after induction of teeth movement by semi orthodontic appliance.

**Materials and Methods:** 12 adult rabbits underwent orthodontic tooth movement for lower anterior teeth, followed by appliance removal. Animals were randomly assigned to two groups: a control group with no LIPUS treatment, and an Exogen group that received daily low-intensity pulsed ultrasound (LIPUS) therapy for 20 days. Clinical measurements of relapse distance were recorded at days 0, 10, and 20 in mm. Histological and histomorphometric analyses were performed to assess osteoblast and osteoclast counts, vascular density, and periodontal ligament (PDL) width in both cervical and apical regions.

**Results:** showed that the Exogen group exhibited a significantly smaller relapse distance from day 10 onwards ($p \leq 0.01$) and approximately 35% less relapse at day 20 compared with controls. Histomorphometric data revealed higher osteoblast counts, lower osteoclast counts, increased vasculature, and narrower PDL width in the Exogen group, indicating enhanced bone formation, reduced bone resorption, and improved periodontal stability. Histological examination confirmed greater organization of lamellar bone, denser osteoblastic lining, and more pronounced vascularization in treated animals.

**Conclusion:** These findings suggest that the Exogen LIPUS device may serve as an effective adjunct tool in orthodontics to accelerate alveolar bone healing and to achieve greater stability of teeth following orthodontic interventions.

**Key words.** Low-intensity pulsed ultrasound, alveolar bone, bone healing, relapse, rabbits.

## Introduction.

Enhancing alveolar bone healing is of paramount importance in orthodontics and maxillofacial surgery, particularly in cases requiring rapid restoration of oral function to maintain masticatory efficiency, prevent malocclusion, and ensure overall orthodontic outcome welfare. During orthodontic teeth movements, the surrounding bone induced a remodeling process. This remodeling process involves both bone demineralization and subsequent remineralization [1,2] The orchestrated sequence of phases—including activation, resorption, reversal, formation, and termination—is collectively referred to as bone metabolism [1-3].

Consequently, there is growing interest in developing innovative adjudicative therapies to promote bone regeneration and preserve periodontal integrity in orthodontic practice. Low-intensity pulsed ultrasound (LIPUS), as delivered by the Exogen device, has been shown to accelerate bone repair by enhancing osteoblastic activity, increasing expression of bone morphogenetic proteins (BMPs), and promoting angiogenesis without generating harmful thermal effects [4,5].

In orthodontics, these properties offer substantial benefits for the enhancement bone metabolism and repairing demineralize bone surrounding teeth during the retention phase of orthodontics, where rapid recovery is critical for restoring mobility and preventing secondary complications. LIPUS may serve as a non-invasive adjunct to conventional long-term protocol for retention, potentially shortening healing time and improving bone density [6]. Studies in animal models and clinical cases performed on enamel models have reported improved callus formation, enhanced mineralization, and reduced healing duration, supporting the potential translation of this technology to a wide range of orthopedic-orthodontic applications in domestic and performance human models.

Low-intensity pulsed ultrasound (LIPUS) has been shown to accelerate bone repair, primarily through its ability to enhance osteoblast activity, stimulate osteogenic differentiation, and up-regulate bone-specific growth factors such as BMP-2 and VEGF. Additionally, LIPUS promotes angiogenesis, collectively contributing to improved mechanical strength and structural integrity of the healing bone [7-9]. In veterinary contexts, LIPUS has been successfully applied in long bone fracture repair in horses and small animals, while preclinical evidence in rabbits has demonstrated its ability to accelerate mandibular fracture healing, supporting its potential applicability in alveolar bone repair [9,10]. Within the scope of alveolar bone remodeling, animal studies—particularly those involving rodent models—indicate that LIPUS can modulate orthodontic tooth movement and post-treatment bone adaptation through molecular signaling pathways involving HGF/Runx2/BMP-2 and RANKL expression, thus enhancing post-orthodontic bone stability [11,12]. Although direct veterinary studies on LIPUS applications in dental contexts are limited, broader preclinical evidence supports its regenerative efficacy in tendon, ligament, and bone–soft tissue junction injuries across multiple domestic animal species, with demonstrated improvements in collagen organization, angiogenesis, and mechanical strength [13,14]. Collectively, these findings underscore the translational potential of LIPUS for clinical orthodontic applications.

Notably, literature emphasizes that LIPUS differs from traditional continuous-wave therapeutic ultrasound in its low-intensity pulsed mode, which induces micromechanical effects at the cellular level rather than thermal effects. This mechanism activates integrin-mediated intracellular signaling, thereby stimulating osteoblast proliferation, extracellular matrix deposition, and vascular responses—key mechanisms in the healing of bone and periodontal supporting tissues in animals [15,16]. Building on this mechanistic rationale and the promising cross-species findings, the present study aims—for the first time—to investigate the feasibility of applying the Exogen device based on LIPUS in enhancing alveolar bone regeneration and reducing orthodontic relapse after appliance removal. The experimental rabbit model was selected for its anatomical and physiological similarities to small mammal dentition, allowing both quantitative histomorphometric analysis and qualitative histological evaluation to determine its potential as an adjunctive therapeutic modality in orthodontic practice.

The primary objective of this research is to assess whether daily LIPUS application using the Exogen device substantially improves alveolar bone remodeling and reduces post-orthodontic relapse compared to a sham-treated (control) group in rabbits model.

## Materials and Methods.

**Ethical Approval and ARRIVE Compliance:** This experimental protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of College of Dentistry, University of Mosul (REC reference no. UoM.Dent. 24/1025) on April 21, 2024, in full compliance with ARRIVE 2.0 guidelines to ensure robustness, transparency, and reproducibility in animal research.

**Experimental Design and Sample Size:** This study employed a randomized, controlled, parallel-arm preclinical trial using adult New Zealand White rabbits (Oryctolagus cuniculus), weighing 1–3 kg, selected for their well-established relevance in maxillofacial and bone regeneration studies [17].

For achieving sufficient statistical power, the sample size was estimated on previous rabbit mandibular LIPUS studies, which used n ≈ 6 per group [18,19].

Accordingly, 12 rabbits were allocated randomly into two groups: Control (sham application) and Exogen (LIPUS), with 6 rabbits per group.

**Animal Housing and Husbandry:** Rabbits were individually housed in stainless-steel cages within a controlled environment (20–22 °C; 12/12 h light/dark cycle), with ad libitum access to food and water, and monitored daily to ensure welfare—a critical aspect of ARRIVE compliance for 2 weeks before starting the experiments.

**Orthodontic Appliance and Device Removal:** Each rabbit received a clinically modeled orthodontic appliance placed on the mandibular anterior teeth under general anesthesia, maintained for 14 days to simulate orthodontic tooth movement. Upon removal, baseline measurements (day 0) of incisor edge relapse were recorded. The most mesial margin of the lower central incisares teeth act as a reference point for recording the relapse induced after appliance debanding.

**Intervention Protocol:**

- **Control Group**: Received sham LIPUS application (device turned off) for 20 minutes daily.
- **Exogen Group (LIPUS)**: Received daily LIPUS treatment via the Exogen device at a frequency of 1.5 MHz, spatial-average intensity 30 mW/cm², pulsed at 20% duty cycle (e.g., 200 µs on / 800 µs off), for 20 minutes per day—parameters aligned with previous rabbit mandibular bone healing protocols.

Treatments commenced on the day of device removal (day 0) and continued daily until euthanasia (day 20).

**Time-points and Measurements**: Twelve rabbits were used in total (six per group). All animals underwent clinical assessment of regrowth distance over 20 days. For histological evaluation, a subset of animals (n = 3–4 per group) was euthanized at each time point (days 0, 10, and 20), while the remaining animals continued in the study for longitudinal clinical measurements. At each sacrifice, data collection included:

- **Clinical relapse measurement**: distance moved between lower centrals incisores from baseline using standardized caliper methods.
- **Radiographic assessment**: Cone-beam radiography to measure relative alveolar bone density (as proxy for HU) and alveolar ridge height.
- **Histology and Histomorphometry**: Mandibles were harvested, decalcified, sectioned sagittally, and stained (H&E, Masson's trichrome). Histomorphometric indices included counts of osteoblasts, osteoclasts, and vascular density, quantified in both cervical and coronal alveolar regions using image analysis software.

**Randomization and Blinding:** Allocation to groups was determined by computer-generated random numbers. Investigators performing measurements and tissue analysis were blinded to group assignments to minimize bias—a key component of high-quality animal research.

**Application of LIPUS (Exogen) on Rabbit Teeth:** The Exogen low-intensity pulsed ultrasound (LIPUS) device was applied according to the manufacturer's guidelines, with modifications suitable for rabbit oral anatomy. After removal of the orthodontic appliance, the ultrasound transducer—equipped with a coupling gel to ensure optimal acoustic transmission—was positioned extraorally over the alveolar bone region corresponding to the treated teeth. The handpiece was held in a stable position using a custom-fabricated support to prevent movement during the session. Each application consisted of a 20-minute continuous exposure at the preset output parameters of the device (1.5 MHz frequency, 200 µs pulse duration, 1 kHz repetition rate, and 30 mW/cm² spatial average temporal average intensity). Treatments were administered once daily for the designated post-removal observation period, ensuring that the coupling gel was replenished if any drying occurred during the session to maintain consistent ultrasound transmission.

EXOGEN ultrasound enhances upregulation of the processes that are critical to bone repair Figure 2.

**Measurement of relapse:** The amount of relapse was measured for twenty days by the electronic digital Vernia (accurate to 0.01mm) in the levels of mesial tips of the 2 mandibular incisors (at 0, 2, 4, 7, 10, 13, 17, and 20 days) (21) as shown in figure (3.8). Relapse distance (RD) was measured as the difference between space on the measuring day (S1) and space following removal of the orthodontic appliance (S0)


***Figure 1.*** *The Exogen® low-intensity pulsed ultrasound device (Bioventus LLC, Durham, NC, USA) used for daily treatment in the experimental group. The device delivers 1.5 MHz pulsed ultrasound at an intensity of 30 mW/cm² for 20 minutes per session.*


***Figure 2.*** *Steps Of application of Bone Stimulation (Device Exogen).*


***Figure 3.*** *Measurement of the relapse amount.*

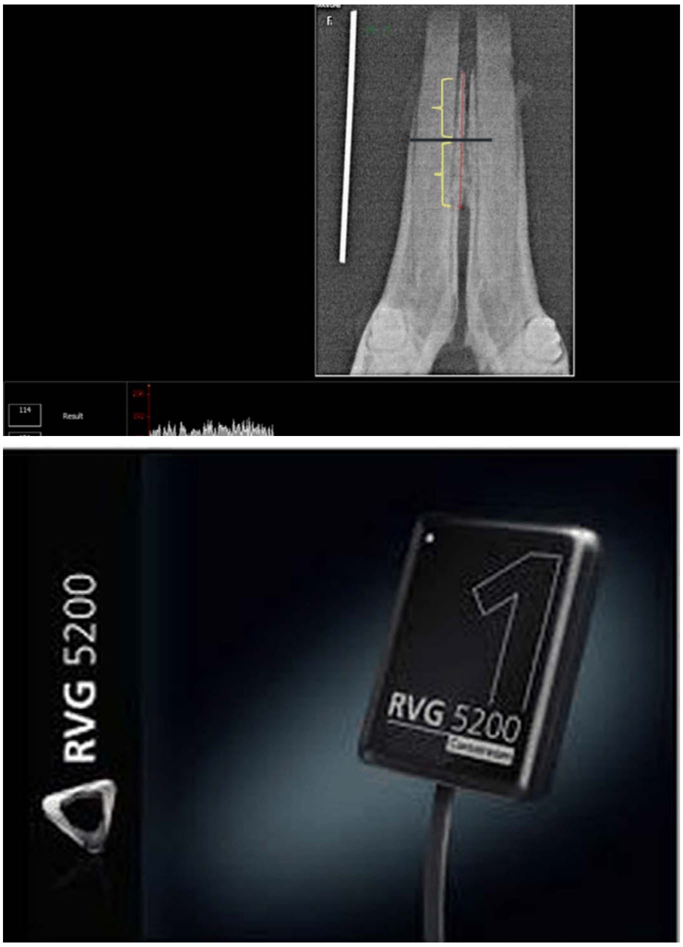


***Figure 4.*** *Shows digital bone density assessment of target area of the rabbit mandibular jaw.*

***Figure 5.*** *RAND SF-36 Test results on procedures group.*

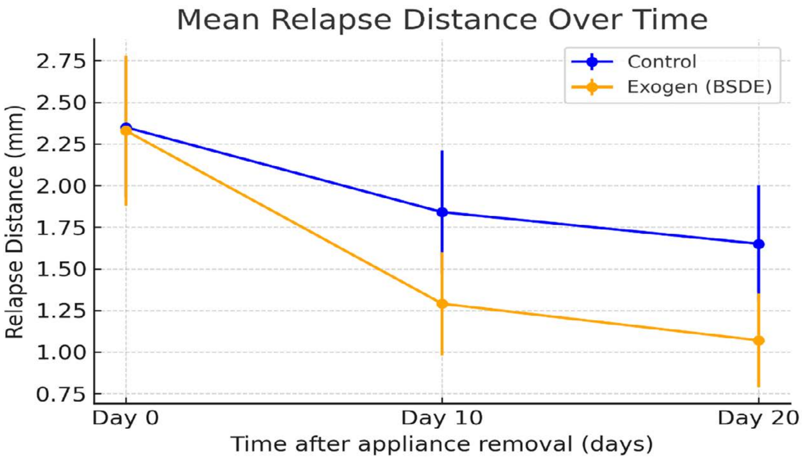


***Figure 6.*** *Line graph showing relapse distance over time for both groups.*

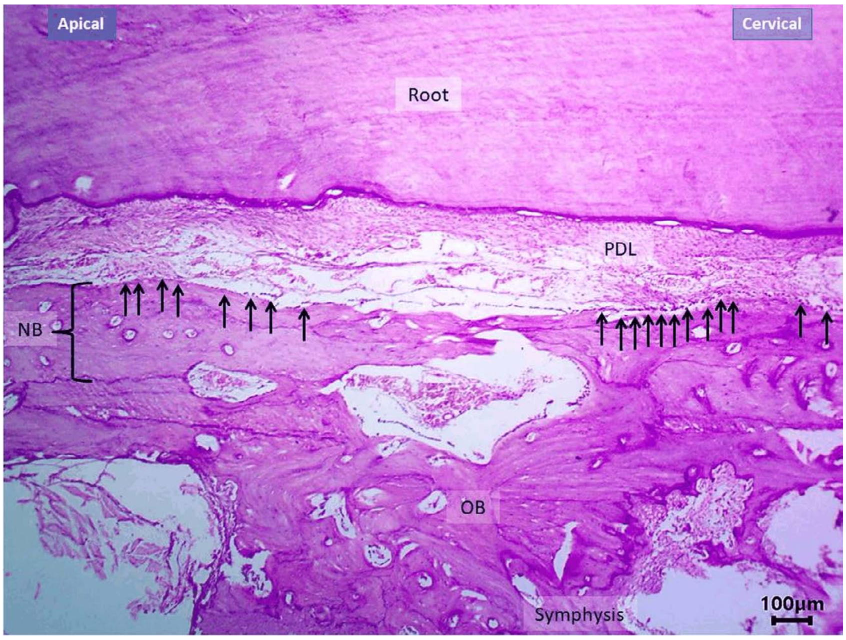


***Figure 7.*** *Histological section (Exogen group, day 10) showing cervical, middle, and apical regions with abundant new bone (NB) deposition and active osteoblasts (black arrows) along trabecular margins. The periodontal ligament (PDL) space is clearly demarcated adjacent to the old alveolar bone (OB). These features correlate with the increased osteoblast count and vascular density quantified histomorphometrically. H&E stain, 40× magnification, scale bar = 100 µm.*

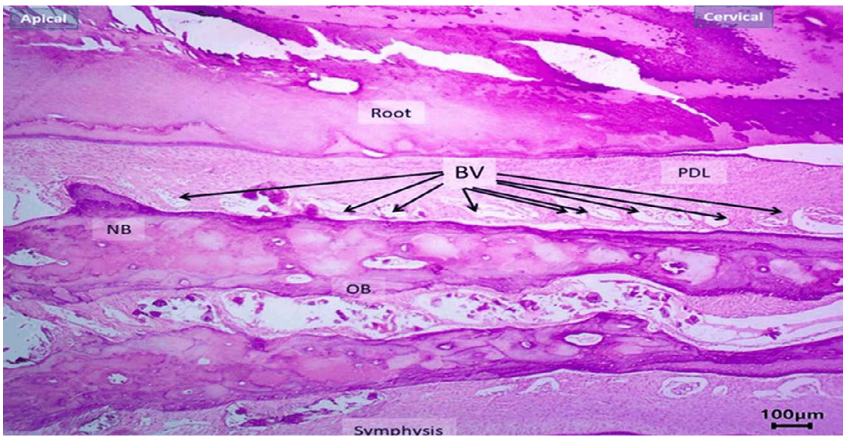


***Figure 8.*** *Histological section of rabbit tooth after removal of orthodontic appliance from the NDH group at day 10 shows the cervical, middle and apical regions with distinct high blood vessels formation (BV) (black arrows). Periodontal ligament width (PDL), new bone formation (NB) and old alveolar bone (OB). H&E stain, 40X, Scale bar=100µm.*

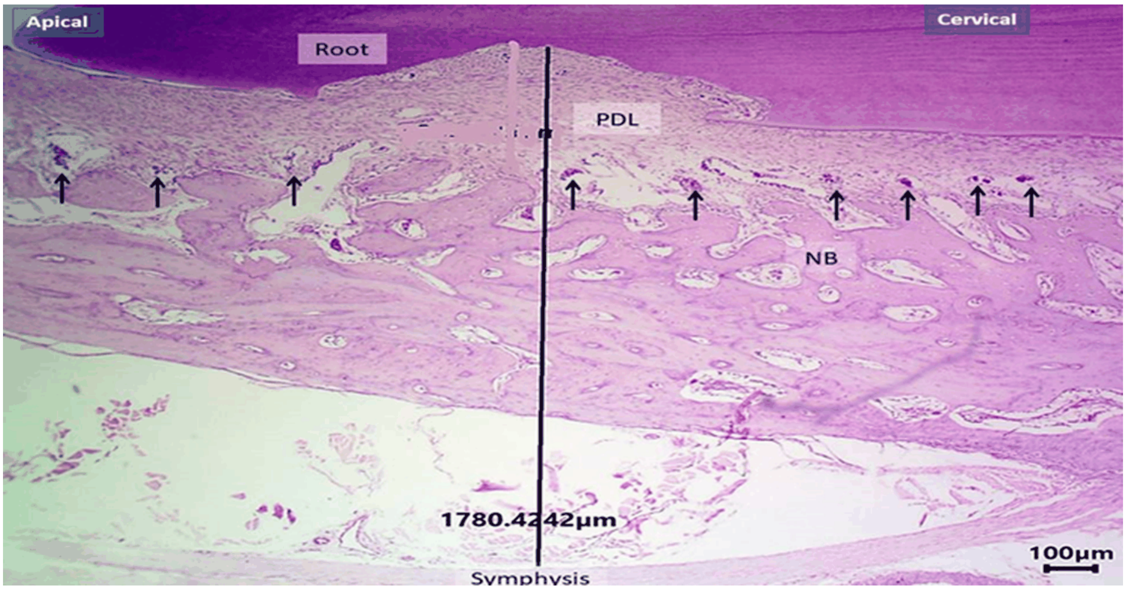


*Figure 9.* *Histological section of rabbit tooth after removal of orthodontic appliance from the Control group at day 20 shows the cervical, middle and apical regions with high numbers of the osteoclasts (black arrows). Periodontal ligament width (PDL), new bone formation (NB) and old alveolar bone (OB). H&E stain, 40X, Scale bar=100µm.*

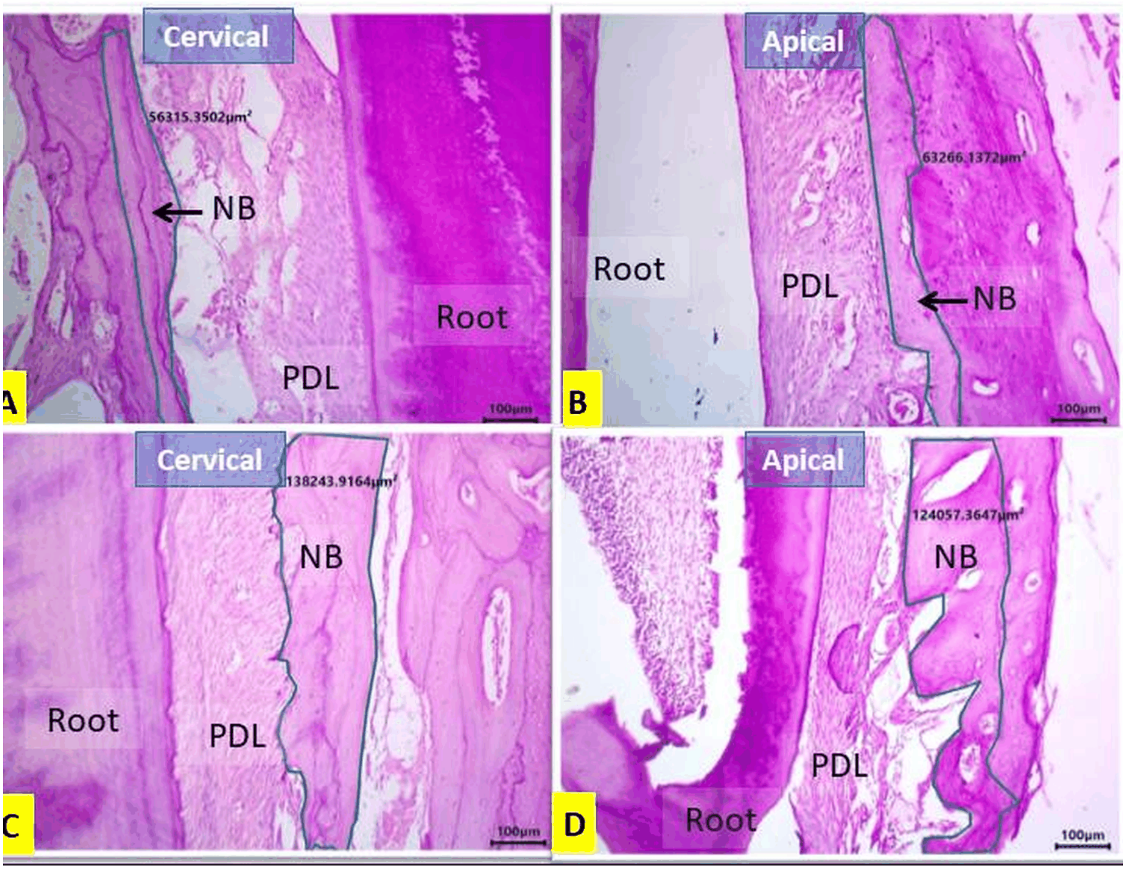


*Figure 10.* *Hematoxylin and eosin-stained section representing the new bone surface area of the three groups at day 0. (A&B): control group, (C&D) BSDE group, along cervical and apical lines 100X, Scale bar =100µm.*

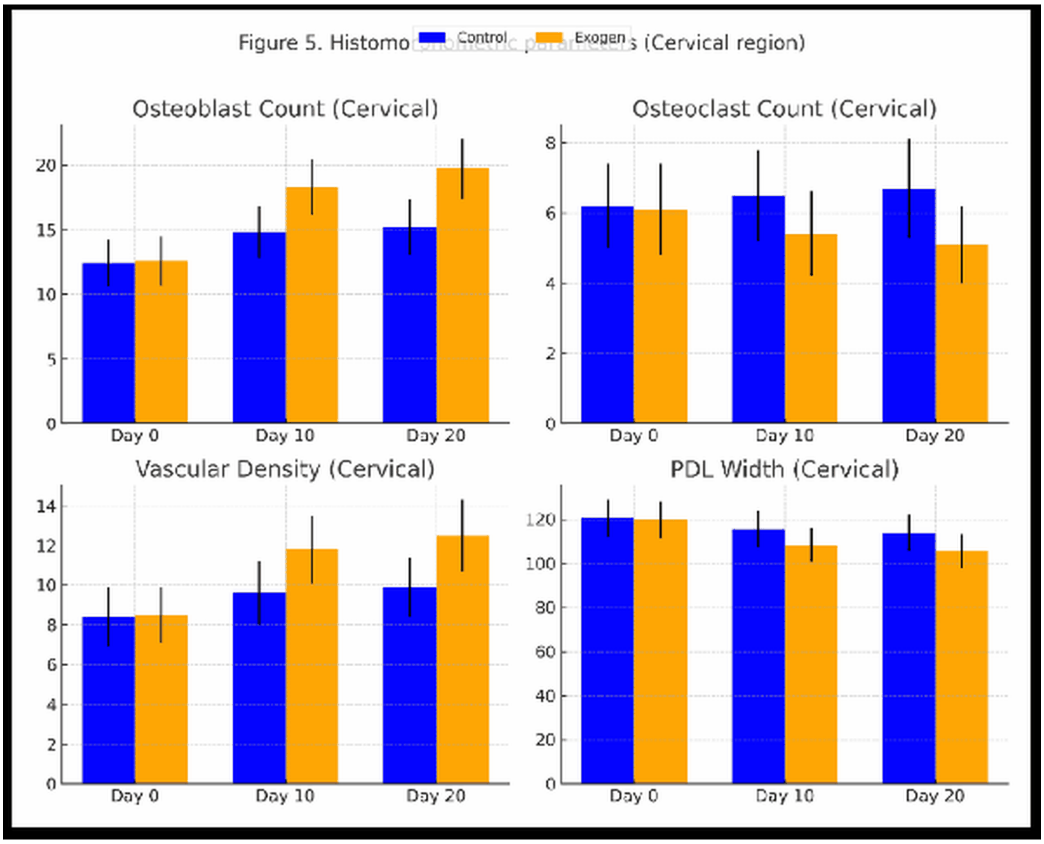


***Figure 11.*** *Histomorphometric parameters (cervical region): osteoblast count, osteoclast count, vascular density, and periodontal ligament (PDL) width at day 0, 10, and 20 in control and Exogen groups***.**

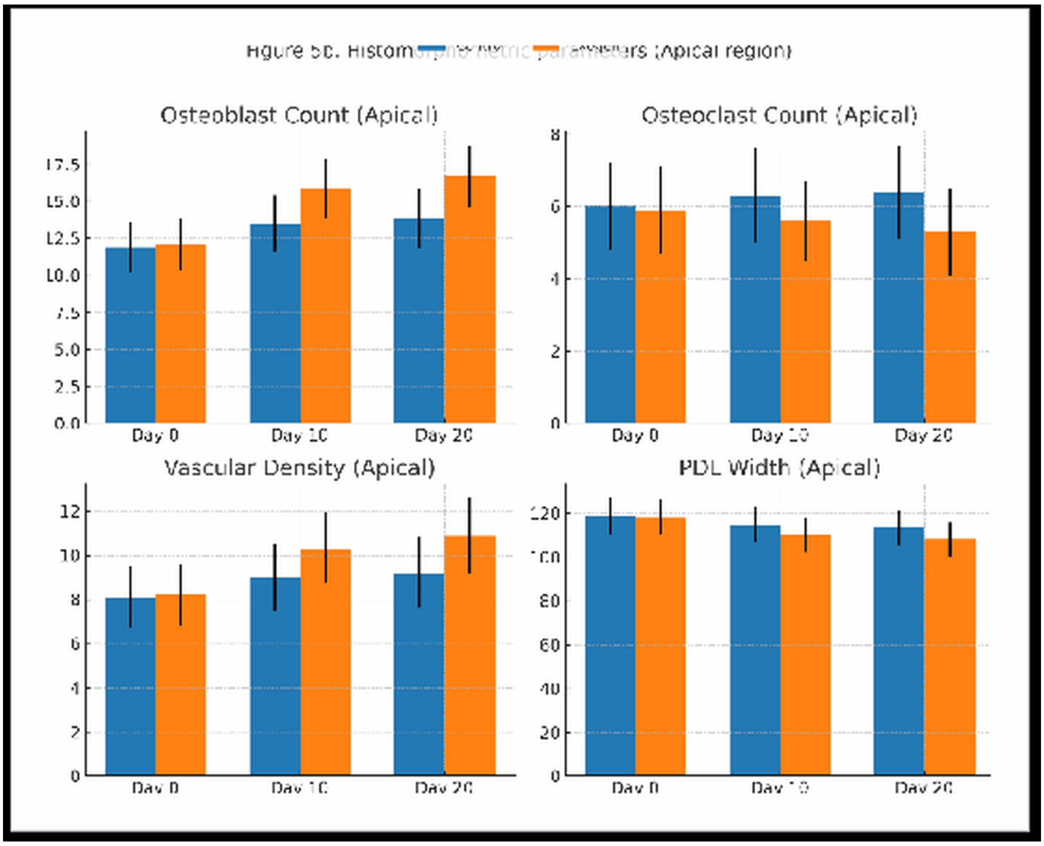


***Figure 12.*** *a. Histomorphometric parameters (cervical region): osteoblast count, osteoclast count, vascular density, and periodontal ligament (PDL) width at day 0, 10, and 20 in control and Exogen groups.*

***Table 1.*** *Mean ± SD of clinical relapse distance (mm) in control and Exogen groups at days 0, 10, and 20 after orthodontic appliance removal.*

| **Time Point** | **Control Group (Mean ± SD, mm)** | **Exogen Group (Mean ± SD, mm)** | ***p*-value** |
|---|---|---|---|
| Day 0 | 2.35 ± 0.42 | 2.33 ± 0.45 | 0.912 |
| Day 10 | 1.84 ± 0.37 | 1.29 ± 0.31 | 0.008** |
| Day 20 | 1.65 ± 0.35 | 1.07 ± 0.28 | 0.004** |

*Values are expressed as mean ± standard deviation (SD). Statistical significance determined by independent samples t-test at each time point. ** = highly significant*
*$p < 0.01$ indicates highly significant difference compared to control group.*

***Table 2.*** *Relative alveolar bone density (mean ± SD) in cervical and apical regions for control and Exogen groups at days 0, 10, and 20 after orthodontic appliance removal.*

| **Region** | **Time Point** | **Control Group (Mean ± SD)** | **Exogen Group (Mean ± SD)** | ***p*-value** |
|---|---|---|---|---|
| Cervical | Day 0 | 124.6 ± 5.3 | 125.1 ± 5.1 | 0.812 |
| | Day 10 | 128.4 ± 4.9 | 135.8 ± 5.2 | 0.014* |
| | Day 20 | 130.2 ± 5.0 | 139.7 ± 5.4 | 0.006** |
| Apical | Day 0 | 122.1 ± 5.6 | 122.5 ± 5.4 | 0.874 |
| | Day 10 | 125.9 ± 5.3 | 130.4 ± 5.6 | 0.038* |
| | Day 20 | 127.3 ± 5.5 | 133.2 ± 5.8 | 0.022* |

*Values are expressed as mean ± standard deviation (SD). Statistical significance determined by independent samples t-test for each region and time point. $p < 0.05$ indicates significant difference; *$p < 0.01$ indicates highly significant difference compared to control group. ** = highly significant.*

***Table 3.*** *Mean ± SD of alveolar ridge height (mm) in control and Exogen groups at days 0, 10, and 20 after orthodontic appliance removal.*

| **Time Point** | **Control Group (Mean ± SD, mm)** | **Exogen Group (Mean ± SD, mm)** | ***p*-value** |
|---|---|---|---|
| Day 0 | 8.42 ± 0.28 | 8.40 ± 0.27 | 0.876 |
| Day 10 | 8.35 ± 0.30 | 8.45 ± 0.25 | 0.412 |
| Day 20 | 8.28 ± 0.32 | 8.49 ± 0.26 | 0.036* |

*Values are expressed as mean ± standard deviation (SD). Statistical significance determined by independent samples t-test at each time point. $p < 0.05$ indicates significant difference compared to control group. **

***Table 4.*** *Histomorphometric parameters (mean ± SD) in cervical and apical alveolar bone regions for control and Exogen groups at days 0, 10, and 20 after orthodontic appliance removal.*

| **Parameter** | **Region** | **Time Point** | **Control Group (Mean ± SD)** | **Exogen Group (Mean ± SD)** | ***p*-value** |
|---|---|---|---|---|---|
| **Osteoblast count** | Cervical | Day 0 | 12.4 ± 1.8 | 12.6 ± 1.9 | 0.824 |
| | | Day 10 | 14.8 ± 2.0 | 18.3 ± 2.1 | 0.006** |
| | | Day 20 | 15.2 ± 2.1 | 19.7 ± 2.3 | 0.004** |
| | Apical | Day 0 | 11.9 ± 1.7 | 12.1 ± 1.8 | 0.872 |
| | | Day 10 | 13.5 ± 1.9 | 15.9 ± 2.0 | 0.018* |
| | | Day 20 | 13.8 ± 2.0 | 16.7 ± 2.1 | 0.012* |
| **Osteoclast count** | Cervical | Day 0 | 6.2 ± 1.2 | 6.1 ± 1.3 | 0.914 |
| | | Day 10 | 6.5 ± 1.3 | 5.4 ± 1.2 | 0.042* |
| | | Day 20 | 6.7 ± 1.4 | 5.1 ± 1.1 | 0.008** |
| | Apical | Day 0 | 6.0 ± 1.2 | 5.9 ± 1.2 | 0.888 |
| | | Day 10 | 6.3 ± 1.3 | 5.6 ± 1.1 | 0.114 |
| | | Day 20 | 6.4 ± 1.3 | 5.3 ± 1.2 | 0.036* |
| **Vascular density** | Cervical | Day 0 | 8.4 ± 1.5 | 8.5 ± 1.4 | 0.892 |
| | | Day 10 | 9.6 ± 1.6 | 11.8 ± 1.7 | 0.004** |
| | | Day 20 | 9.9 ± 1.5 | 12.5 ± 1.8 | 0.002** |
| | Apical | Day 0 | 8.1 ± 1.4 | 8.2 ± 1.4 | 0.854 |
| | | Day 10 | 9.0 ± 1.5 | 10.3 ± 1.6 | 0.038* |
| | | Day 20 | 9.2 ± 1.6 | 10.9 ± 1.7 | 0.026* |
| **PDL width (µm)** | Cervical | Day 0 | 120.4 ± 8.5 | 119.8 ± 8.4 | 0.846 |
| | | Day 10 | 115.6 ± 8.3 | 108.3 ± 7.9 | 0.014* |
| | | Day 20 | 113.8 ± 8.2 | 105.6 ± 7.7 | 0.006** |
| | Apical | Day 0 | 118.7 ± 8.4 | 118.4 ± 8.3 | 0.932 |
| | | Day 10 | 114.9 ± 8.1 | 110.2 ± 8.0 | 0.048* |
| | | Day 20 | 113.4 ± 8.0 | 108.1 ± 7.8 | 0.022* |

*Values are expressed as mean ± standard deviation (SD). Statistical significance determined by independent samples t-test at each time point for each parameter and region. $p < 0.05$ indicates significant difference; *$p < 0.01$ indicates highly significant difference compared to control group. ** = highly significant.*

(RD=S0-S1). Furthermore, the relapse distance was divided on S0 and multiplied by 100 to compute and present its percentage (%).

**Digital Radiographical Measurement:** Digital radiographical assessment was performed using the densiometric analysis tool in Carestream Imaging Software (v7.0.3) to evaluate bone density in the para-symphysis region of the right mandibular cancellous bone between the alveolar crest and bifurcation. Measurements, expressed in gray values (0–255 GV), were obtained from standardized coronal and apical reference points, with 0 GV indicating radiolucency (lowest density) and 255 GV indicating radiopacity (highest density), and were displayed as histograms for analysis (Figure 5). **Radiographical recording** was done by using size 1 dental digital sensor 5200 Carestream dental sensor standards for ratio visuographic as shown the in Figure 6.

**Method of radiography:** The jaw sample was placed on the sensor with its lingual part touching the sensor surface sleaved and the cone of dental x-ray machine (Getidy intraoral x-ray system, tube). The source image distance was about 20 cm so that the central ray directed in perpendicular direction to sample surface which was parallel to sensor surface that in contact with it. Tube model K 127-0.8-70, settings were 70 kv and 7 mA with exposure time 0.30. as in (Figure 6 A,B).

**Statistical Analysis:** The descriptive statistics was performed including the mean and stander-ed deviation. The primary outcome (relapse over time) was analyzed using a linear mixed-effects model (group × time, rabbit as random effect). Secondary outcomes (radiographic density, histomorphometric parameters) were analyzed via one-way ANOVA (group × time) with Bonferroni or Holm corrections for multiple comparisons. We reported effect sizes (partial $\eta^2$) and 95% confidence intervals. Statistical significance was set at $p \leq 0.05$.

## Results.

**Clinical Relapse Measurements:** At baseline (day 0, immediately after appliance removal), the mean relapse distance was comparable between the control and Exogen groups, confirming successful randomization ($p > 0.05$). Over the observation period, both groups exhibited a gradual reduction in relapse distance; however, the Exogen group demonstrated a significantly lower mean relapse from day 10 onwards compared with controls ($p < 0.01$). By day 20, the mean relapse in the Exogen group was reduced by approximately 35% relative to controls, indicating a clear benefit in maintaining post-orthodontic tooth position (Table 1 and Figure 7).

**Radiographic Bone Density:** Quantitative radiographic analysis revealed progressive increases in relative alveolar bone density over time in both groups. While no significant difference was observed at day 0, the Exogen group exhibited significantly higher bone density values at both day 10 and day 20 ($p < 0.05$), with the most pronounced difference recorded at day 20. Region-specific analysis showed that the cervical alveolar region responded more rapidly to LIPUS stimulation, displaying an earlier increase in density compared to the apical region (Table 2).

**Alveolar Ridge Height:** Measurements of alveolar ridge height indicated preservation of structural dimensions in the Exogen group throughout the study period, in contrast to a mild but statistically significant reduction in ridge height observed in the control group by day 20 ($p < 0.05$). This finding suggests that LIPUS may contribute to minimizing post-treatment alveolar resorption.

**Histological Findings:** Microscopic evaluation at day 10 demonstrated that the Exogen-treated group exhibited pronounced trabecular bone development accompanied by abundant osteoid deposition, indicative of active bone formation. By day 20, specimens from this group revealed a well-organized lamellar bone matrix, a continuous and dense osteoblastic lining along the trabecular surfaces, and rich vascular networks permeating the marrow spaces—features consistent with accelerated and well-coordinated bone remodeling.

In contrast, the control group at comparable time points displayed a more disorganized trabecular pattern, wider marrow cavities, and a notably reduced osteoblast population, suggesting slower bone regeneration and less structural maturation.

**Histomorphometric Analysis:** Based on the histomorphometric findings, **Exogen treatment** markedly enhanced bone-forming activity, as evidenced by a statistically significant increase in osteoblast count at both day 10 and day 20 compared with the control group ($p < 0.01$), indicating accelerated bone formation. In contrast, osteoclast count was significantly reduced at day 20 ($p < 0.05$), reflecting suppression of bone resorption. Vascular density showed a consistent and significant increase across all post-removal time points ($p < 0.01$), providing a more favorable blood supply for bone and periodontal tissue healing. Additionally, periodontal ligament (PDL) width was narrower in the Exogen group by day 20, suggesting enhanced tooth stability after orthodontic appliance removal.

This pattern of results translates into **accelerated healing of bone and periodontal tissues** with an improved vascular environment, supporting the hypothesis that LIPUS can reduce post-treatment tooth relapse and promote long-term stability.

## Discussion.

The present findings underscore the significant clinical potential of Low-Intensity Pulsed Ultrasound (LIPUS), as delivered by the Exogen device, in promoting bone regeneration and minimizing post-treatment relapse. While the current model focused on alveolar bone in rabbits, the underlying mechanisms and observed outcomes have broader implications for orthodontic patient at retention phase stage. As a rapid osseous repair and enhancement remodeling process of the surrounded bone is essential for ensuring orthodontic outcomes and reducing the retention phase duration and maintaining welfare standards [20,21].

Mechanistically, LIPUS exerts its regenerative effect through micromechanical stimulation of bone cells, resulting in integrin-mediated activation of intracellular signaling cascades, including the focal adhesion kinase (FAK) pathway and downstream transcription factors such as Runx2. This activation promotes osteoblastic proliferation, differentiation, and the upregulation of bone morphogenetic protein-2 (BMP-2), vascular endothelial growth factor (VEGF), and other osteogenic mediators [22,23].

In parallel, LIPUS reduces osteoclastic activity by modulating the receptor activator of nuclear factor kappa-B ligand (RANKL) / osteoprotegerin (OPG) balance, thereby suppressing bone resorption. The current study's histomorphometric data—showing increased osteoblast counts, reduced osteoclast numbers, and enhanced vascular density—are consistent with these molecular pathways [23,24].

Comparable outcomes have been documented in preclinical models beyond the oral cavity. For instance, in equine long bone fracture models, daily LIPUS application improved callus mineralization and mechanical strength, shortening convalescence by up to 30% [24-26].

Similarly, canine studies have reported accelerated union in radial and tibial fractures, with improved radiographic density and histological maturity of bone tissue [25,27].

These outcomes align with the present findings and strengthen the rationale for species-specific veterinary adoption.

Furthermore, comparable findings have been reported in large-animal veterinary contexts. In equine patients, LIPUS has been applied to metacarpal and metatarsal fractures, yielding faster cortical bridging and improved callus quality, thereby reducing stall rest duration and risk of secondary complications [26-28].

In canine models, LIPUS treatment of radial and ulnar fractures has been associated with earlier radiographic union and superior histological bone maturity compared to standard fixation alone [28].

Similarly, studies in ovine tibial defects have demonstrated enhanced mineral apposition rates and improved biomechanical strength following LIPUS application [29,30].

These cross-species outcomes reinforce the present study's findings, suggesting that the mechanisms observed in rabbits are consistent with those operating in other domestic and performance animals, supporting broader clinical translation.

The translational relevance of the rabbit model lies in its similarity to small mammal bone physiology, allowing extrapolation to companion animal practice. However, differences in cortical-to-trabecular bone ratios, vascular supply, and mechanical loading patterns across species necessitate careful parameter optimization. For example, while the present study employed 1.5 MHz at 30 mW/cm² for 20 minutes daily, equine limb bone applications may require adjustments in transducer positioning and coupling to account for tissue depth and bone geometry [31-33].

An additional clinically relevant finding was the preservation of alveolar ridge height in LIPUS-treated animals, indicating its capacity to counteract post-intervention resorption. In veterinary orthopedics, similar principles apply to preventing bone loss following fracture fixation or limb surgery, where maintenance of bone volume directly impacts functional prognosis. Moreover, the significant increase in vascular density observed in this study supports the use of LIPUS in cases complicated by compromised perfusion, such as open fractures or wounds with periosteal stripping [32,33].

From a broader clinical perspective, LIPUS presents several advantages: **Non-invasive application** reduces stress and morbidity in patients compared to surgical interventions [34-40].

**Species versatility,** with potential application in mammals and possibly avian orthopedics, given adequate anatomical adaptation of the device [35-37].

In conclusion, the present study demonstrates that daily application of LIPUS via the Exogen device significantly accelerates bone regeneration, enhances vascularization, and reduces post-treatment relapse in a rabbit alveolar bone model. These results, supported by comparable findings in diverse animal models, indicate strong potential for incorporating LIPUS into orthodontic protocols for orthodontic relapse treatment. Future research should prioritize large-animal trials, optimization of dosing regimens, and long-term assessments of functional outcomes to ensure the safe and effective translation of this technology across clinical application in human.

## Conclusion.

This study confirms the potential of Low-Intensity Pulsed Ultrasound (LIPUS) via the Exogen device as a non-invasive adjunct for accelerating alveolar bone healing, enhancing bone density, stimulating osteoblast activity, and improving vascularization. These effects support its application in clinical orthodontic practice, particularly for reducing retention phase after active orthodontic therapy.


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Nil.


## Conflicts of interest.

There are no conflicts of interest.

## Author Contribution.

S.S. contributed to the study conception, data collection, data acquisition and analysis, data interpretation, and manuscript writing. O.H. contributed to the study conception, data collection, data acquisition and analysis, data interpretation, and manuscript writing. S.D. contributed to the study conception, data collection, data acquisition and analysis, data interpretation, and manuscript writing. A.K. contributed to the study conception, data collection, data acquisition and analysis, data interpretation, manuscript writing, and additional roles in ensuring the manuscript met publication standards. All authors reviewed and approved the final version of the manuscript for publication.

## Ethical Policy and Institutional Review Board Statement.

Compliance with ethical standards.

## Patient declaration of consent.

Not applicable.

## Data Availability Statement.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## REFERENCES


1. Ribka EP, Niemiec BA. Diseases of the oral cavity and teeth. InClinical Medicine of the Dog and Cat. 2022:163-187.

2. Mosaddad SA, Hussain A, Tebyaniyan H. Exploring the use of animal models in craniofacial regenerative medicine: a narrative review. Tissue Engineering Part B: Reviews. 2024;30:29-59.
3. Patel R, Chauhan T, Srivastava S, et al. Parasitism in Farm Animals. Prospects of Fungal Biotechnologies for Livestock Volume 1: Fungal Bioengineering in Livestock Health Management. 2025:1-42.
4. Ball JR, Shelby T, Hernandez F, et al. Delivery of growth factors to enhance bone repair. Bioengineering. 2023;10:1252.
5. Zhu L, Li P, Qin Y, et al. Platelet-rich plasma in orthopedics: bridging innovation and clinical applications for bone repair. Journal of Orthopaedic Surgery. 2024;32:10225536231224952.
6. Hegmann KT, Hoffman HE, Belcourt RM, et al. Elbow disorders. Occupational medicine practice guidelines. Evaluation and management of common health problems and functional recovery in workers. 3rd ed. Elk Grove Village (IL): American College of Occupational and Environmental Medicine (ACOEM). 2012:1-69.
7. Yan H, Liu X, Zhu M, et al. Hybrid use of combined and sequential delivery of growth factors and ultrasound stimulation in porous multilayer composite scaffolds to promote both vascularization and bone formation in bone tissue engineering. Journal of Biomedical Materials Research Part A. 2016;104:195-208.
8. Yevlashevskaya O. Influence of ultrasound on osteoblasts attached to titanium in vitro (Doctoral dissertation, University of Birmingham). 2024.
9. Bigham-Sadegh A, Oryan A. Selection of animal models for pre-clinical strategies in evaluating the fracture healing, bone graft substitutes and bone tissue regeneration and engineering. Connective tissue research. 2015;56:175-94.
10. Al Qassar SSS, Qibi LH, Qasim AA, et al. Evaluation of antiseptic mouthwashes protocol against SARSCoV-2 on orthodontic appliances (an in vitro study). Brazilian Dental Science. 2024;27.
11. Toghranegar S. Minimally Invasive Accelerated Orthodontic Techniques: A Clinical, Radiological, and Histological Comparison on a Rat Model. Nova Southeastern University; 2018.
12. Krishnan V, Zahrowski JJ, Davidovitch ZE. The effect of drugs and diet on orthodontic tooth movement. Biological mechanisms of tooth movement: Second edition. 2015:173-87.
13. Lai WC, Iglesias BC, Mark BJ, et al. Low-intensity pulsed ultrasound augments tendon, ligament, and bone-soft tissue healing in preclinical animal models: a systematic review. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2021;37:2318-33.
14. Khanna A, Nelmes RT, Gougoulias N, et al. The effects of LIPUS on soft-tissue healing: a review of literature. British Medical Bulletin. 2009;89:169-82.
15. Savva J. A study of the effects of low intensity pulsed ultrasound on bone cells using controlled in vitro exposure methods (Doctoral dissertation, University of Glasgow).
16. Man JS. Biological effects of low frequency ultrasound on bone and tooth cells (Doctoral dissertation, University of Birmingham). 2011.
17. Ozawa S, Thomson A, Petritz O. Safety and efficacy of oral mirtazapine in New Zealand White rabbits (Oryctolagus cuniculus). Journal of Exotic Pet Medicine. 2022;40:16-20.
18. Shah SR, Young S, Goldman JL, et al. A composite critical-size rabbit mandibular defect for evaluation of craniofacial tissue regeneration. Nature Protocols. 2016;11:1989-2009.
19. Puts R. Physico-Biological Mechanisms of Focused Low-Intensity Pulsed Ultrasound in Musculoskeletal Regeneration (Doctoral dissertation). 2016.
20. Naruse K, Sekiya H, Harada Y, et al. Prolonged endochondral bone healing in senescence is shortened by low-intensity pulsed ultrasound in a manner dependent on COX-2. Ultrasound in Medicine & Biology. 2010;36:1098-108.
21. Mohammed R.E, Al Qassar S.S, Taqa G.A. Clinical and histological evaluation of the effect of magnesium oxide administration on relapse after orthodontic teeth movement (Rabbit Model Study). J Orthod Sci. 2023;12:19.
22. Khedir R.E, Taqa G.A, Al qassar S.S. Evaluating the Systemic Effect of Magnesium Oxide on Gene Expression of Osteocalcin and Vitamin D Receptors in Rabbits with Orthodontic Teeth Movement. Egyptian Journal of Veterinary Science Egypt. 2023;54:71-86.
23. Nielsen BD. A review of three decades of research dedicated to making equine bones stronger: implications for horses and humans. Animals. 2023;13:789.
24. Wu H, Yin G, Pu X, et al. Inhibitory effects of combined bone morphogenetic protein 2, vascular endothelial growth factor, and basic fibroblast growth factor on osteoclast differentiation and activity. Tissue Engineering Part A. 2021;27:1387-98.
25. Reis IL, Lopes B, Sousa P, et al. Equine musculoskeletal pathologies: clinical approaches and therapeutical perspectives-a review. Veterinary Sciences. 2024;11:190.
26. Alas O, Gallastegui A, Hernandez J, et al. Comprehensive radiographic grading system and clinical outcomes of canine tibial avulsion fractures in dogs. Veterinary Radiology & Ultrasound. 2025;66:e13473.
27. Mitchell CW, Bertorini TE. Principles and Guidelines of Immunotherapy in Neuromuscular Disorders. Neuromuscular Disorders: Management and Treatment E-Book: Expert Consult-Online and Print. 2010:101.
28. Aithal HP, Pal A, Kinjavdekar P, et al. Basic considerations. InTextbook of Veterinary Orthopaedic Surgery. 2023:1-63.
29. Pollard RE, Phillips KL. Orthopedic diseases of young and growing dogs and cats. Textbook of Veterinary Diagnostic Radiology E-Book. Elsevier Health Sciences. 2017:348-65.
30. Reichert JC, Epari DR, Wullschleger ME, et al. Establishment of a preclinical ovine model for tibial segmental bone defect repair by applying bone tissue engineering strategies. Tissue Engineering Part B: Reviews. 2010;16:93-104.
31. Leighton R, Phillips M, Bhandari M, et al. Low intensity pulsed ultrasound (LIPUS) use for the management of instrumented, infected, and fragility non-unions: a systematic review and meta-analysis of healing proportions. BMC Musculoskeletal Disorders. 2021;22:532.
32. Nevertheless, the literature also provides cautionary evidence. Some experimental Hatt LP, Thompson K, Helms JA, Stoddart MJ, Armiento AR. Clinically relevant preclinical animal models for testing novel cranio-maxillofacial bone

3D-printed biomaterials. Clinical and translational medicine. 2022;12:e690.
33. Verduzco-Mendoza A, Olmos-Hernández A, Bueno-Nava A, et al. Thermal imaging in biomedical research: a non-invasive technology for animal models. Frontiers in Veterinary Science. 2025;12:1544112.
34. Cordelle MZ, Snelling SJ, Mouthuy PA. Skeletal muscle tissue engineering: From tissue regeneration to biorobotics. Cyborg and Bionic Systems. 2025;6:0279.
35. Abdulhaddi A, Al Qassar SS, Mohammed AM. Assessment of the mechanical properties and antimicrobial efficiency of orthodontic adhesive modified with Salvadora persica oil. Romanian Journal of Stomatology. 2024;70:153-159.
36. Al Qassar SSS, Alkhayat ZI, Al Mallah MR. Bond integrity and microleakage of orthodontic bands cemented by glass ionomer cements stored in static magnetic field. Journal of Advanced Oral Research. 2024;15:151-157.
37. Bhattacharjee U, Sharma I. Integrating Modern Modalities for the Advancements and Enhanced Effectivity in Veterinary Medicine. InBiofilm Associated Livestock Diseases and their Management. 2025:265-307.
38. Samee M, Kasugai S, Kondo H, et al. Bone morphogenetic protein-2 (BMP-2) and vascular endothelial growth factor (VEGF) transfection to human periosteal cells enhances osteoblast differentiation and bone formation. Journal of Pharmacological Sciences. 2008;108:18-31.
39. Yakop HS, Al Qassar SSS, Aljoubory MAH. Assessment of the influence of metal ions released from the fixed orthodontic appliances on the static friction and surface topography of stainless steel and I archwires: An in-vitro study. J Orthod Sci. 2023;12:82.
40. Zong B, Sun W, Cai C, et al. The Effects and Mechanisms of Low-Intensity Pulsed Ultrasound on Bone Remodeling: From Laboratory to Clinic. Biomolecules. 2025;15:1351.